DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our STN: BL 103949 (replaces Ref. No. 99-1488)

January 19, 2001

Nicholas J. Pelliccione, Ph.D.
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Pelliccione:

Your biologics license application for Peginterferon alfa-2b is approved effective this date. Schering Corporation, Kenilworth, New Jersey, is hereby authorized to introduce or deliver for introduction into interstate commerce, Peginterferon alfa-2b under Department of Health and Human Services U.S. License No. 0994.

Peginterferon alfa-2b is indicated for the treatment of chronic hepatitis C in patients not previously treated with interferon alfa who have compensated liver disease and are at least 18 years of age. Under this authorization, you are approved to manufacture Peginterferon alfa-2b at your facility in Innishannon County Cork, Ireland. Final formulated drug product will be filled at Innishannon County Cork and unlabeled vials of drug product will be shipped to Kenilworth, New Jersey, for labeling, packaging and distribution. In accordance with approved labeling, your product will bear the trade name PEG-Intron, and will be marketed in 100 µg /mL, 160 µg /mL, 240 µg /mL and 300 µg /mL vials of lyophilized powder, supplied with a 5-mL vial of PEG-Intron Diluent (Sterile Water for Injection), two disposable 1-mL (Becton Dickenson Safety-Lok) syringes with needles and needle guards, and alcohol swabs.

The dating period for Peginterferon alfa-2b shall be 24 months from the date of manufacture when stored at 25 °C (77 ° F). The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The bulk drug substance may be stored for up to 36 months at -80 °C. Results of ongoing stability studies should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots. The stability protocol in your license application is considered approved for the purpose of extending the expiration dating period of your drug substance and drug product as specified in 21 CFR 601.12.

You are not currently required to submit samples of future lots of Peginterferon alfa-2b to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2. FDA will continue to monitor compliance with 21 CFR 610.1 requiring assay and release of only those lots that meet release specifications.

Any changes in the manufacturing, testing, packaging or labeling of Peginterferon alfa-2b, or in the manufacturing facilities will require the submission of information to your biologics license application for our review and written approval consistent with 21 CFR 601.12.

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As of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We do not concur with your request, as submitted to your application on February 4, 2000, to waive the requirement to conduct pediatric studies. As communicated during the December 14, 2000, meeting, we are deferring the submission of your pediatric studies until June 30, 2001, subsequent to discussion at an open session of an FDA advisory committee meeting.

Pursuant to 21 CFR Part 208, FDA has determined that this product poses a serious and significant public health concern requiring the distribution of a Medication Guide. Distribution of a Medication Guide is necessary for safe and effective use of this product. FDA has determined that Peginterferon alfa-2b is a product for which patient labeling could help prevent serious adverse effects and inform the patient of serious risks relative to benefit that could affect their decisions to use, or continue to use the product. *See* 21 CFR 208.1. FDA hereby approves the Medication Guide you submitted January 19, 2001. In accordance with 21 CFR 208, you are responsible for ensuring that this Medication Guide is available for every patient who is dispensed a prescription for this product. In addition, you are responsible for ensuring that the label of each package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided.

We acknowledge your written commitments to provide additional information and to conduct post marketing studies as described in your letters of November 28, 2000, and January 12, 2001, as outlined below:

1. To address the safety and efficacy of Peginterferon alfa-2b in African Americans by submitting the data from a study of 100 previously untreated patients with chronic hepatitis C who will receive 1.5 µg/kg PEG-Intron and 800, 1000 or 1200 mg ribavirin, depending on their weight. The final protocol for this study will be submitted to CBER by April 1, 2001. Patient accrual will be completed by June 1, 2002, the study completed by December 1, 2003 and a final study report submitted to CBER by June 1, 2004.

2. To evaluate, in patients diagnosed with chronic hepatitis C and compensated liver disease, the effects of single and multiple doses of Peginterferon alfa-2b on the disposition of drugs known to be metabolized by hepatic cytochrome P450 enzymes. The final protocol for this study will be submitted to CBER by February 22, 2001. Patient accrual will be completed by February 19, 2002, the study completed by April 19, 2002, and a final study report submitted to CBER by November 20, 2002.

3 To evaluate the pharmacokinetic, pharmacodynamic and clinical effects of Peginterferon alfa-2b when given chronically to patients with renal dysfunction (creatinine clearance < 50 mL/min). The final protocol for this study will be submitted to CBER by March 1, 2001. Patient accrual will be completed by March 1, 2002, the study completed by April 29, 2002, and a final study report submitted to CBER by October 21, 2002.

4 To evaluate the pharmacokinetic, pharmacodynamic and clinical effects of Peginterferon alfa-2b when administered to patients receiving methadone. The final protocol for this study will be submitted to CBER by May 15, 2001. Patient accrual will be completed by May 12, 2004, the study completed by July 12, 2004, and a final study report submitted to CBER by January 18, 2005.

5 To replace the 5-mL vial of diluent that is packaged with Peginterferon alfa-2b with a 1-mL vial of diluent. The supplement supporting this change will be submitted by December 31, 2001.

It is requested that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2567 or Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Sincerely yours,

Shawn L Russo

for Jay P. Siegel, M.D., FACP
Director
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research